ANG 0 2 2002 STATES PATENT AND TRADEMARK OFFICE

In re application of:

BEUG et al.

Appl. No. 10/086,073

Filing Date: March 1, 2002

For: Pharmaceutical Compositions for Treating Tumour Diseases

Confirmation No: 3217

Art Unit:

1642

Examiner:

To be assigned

Walter State of the State of th

Atty. Docket: 0652.1790001/EKS/BEC

Information Disclosure Statement

Assistant Commissioner for Patents Washington, D.C. 20231

Sir:

Listed on accompanying Form PTO-1449 are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98. A copy of each of these documents is provided.

Document AP1 is in the German language with an English language abstract. The relevance of document AP1 can be ascertained by reference to page 26, lines 23-25, of the application as filed.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicants have listed publication dates on the attached PTO-1449 based on information presently available to the undersigned. However, the listed publication dates should not be construed as an admission that the information was actually published on the date indicated.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

BEUG *et al.* Appl. No. 10/086,073

- 2 -

This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent application does not exist. The Examiner is specifically requested not to rely solely on the material submitted herewith. It is further understood that the Examiner will consider information that had been cited or submitted to the U.S. Patent and Trademark Office in a prior application relied on under 35 U.S.C. § 120. 1138 OG 37, 38 (May 19, 1992).

This Information Disclosure Statement is being submitted more than three months after the filing date, but before the first mailing of an Office Action on the merits. No statement or fee is required.

It is respectfully requested that the Examiner initial and return a copy of the enclosed PTO-1449, and to indicate in the official file wrapper of this patent application that the documents have been considered.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Br E. Clellan

Bruce E. Chalker Attorney for Applicants Registration No. 47,480

Date: August 2, 2002

1100 New York Avenue, N.W. Suite 600 Washington, D.C. 20005-3934 (202) 371-2600

::ODMA\MHODMA\SKGF_DC1;33209;1 SKGF Rev. 1/26/98 clp

Page 1 of 19 ATTY. DOCKET NO. APPLICATION NO. 0652.1790001/EKS/BEC 10/086,073 FORM PTO-1449 APPLICANTS Beug et al. INFORMATION DISCLOSURE STATEMENT GROUP FILING DATE March 1, 2002 1642 U.S. PATENT DOCUMENTS EXAMINER FILING DATE CLASS SUB-DOCUMENT DATE NAME TNTTTAL NUMBER CLASS AA AB AC ΑD ΑE AF AG AΗ ΑI ΑJ ΑK FOREIGN PATENT DOCUMENTS EXAMINER CLASS SUB-TRANSLATION COUNTRY DOCUMENT DATE INITIAL CLASS NUMBER Yes WIPC 12, 26, 1991 WO 91/19513 No AL1 Α1 Yes 06, 29, 1994 Europe EP 0 604 181 AM1 A1 Yes 11:10/1994 WIPO WO 94/25588 No AN1 A2 Yes WITEO 07 27,1995 WO 95/19987 No A01 Α1 Yes 03 '14/1996 CITW WO 96/07657 No AP1 Α1 OTHER (Including Author, Title, Date, Pertinent Pages, etc.) Andrejauskas, E., and Moroni, C., "Reversible abrogation of IL-3 dependence by an inducible H-ras oncogene," $\it EMBO\ J.\ 8:2575-2581$, IRL Press (1989) AR 1 Antonelli-Orlidge, A., et al., "An activated form of transforming growth factor β is produced by cocultures of endothelial cells and pericytes, " Proc. Natl. Acad. AS 1 Sci. USA 86:4544-4548, National Academy Press (1989) Beham, A., et al., "Distribution of cytokeratins, vimentin and desmoplakins in normal renal tissue, renal cell carcinomas and oncocytoma as revealed by ΑТ immunofluorescence microscopy, " Virchows Archiv. A Pathol. Anat. 421:209-215, <u>1</u> Springer-Verlag (1992) DATE CONSIDERED EXAMINER

Page 2 of 19

FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO. 0652.1790001/EKS/BEC	APPLICATION NO. 10/086,073
APPLICANTS Beug et al.	
	GROUP

INFORMATION DISCLOSURE STATEMENT				2349						
1101	OKMATIO	DIOC	2000		FILING DATE	FILING DATE GROUP March 1, 2002 1642				
			 	TI TI	S. PATENT DOCUMENTS		<u> </u>			
				_ 	S. PAIDAT DOCUMENTS					
EXAMINER INITIAL		DOCU NUMB	MENT ER	DATE	NAME	CL	ASS	SUB- CLASS	FILING DATE	
	AA								10	
	AB							- 31	EN-	
	AC	ļ						CE11	1-1900,5300 5005	
	AD					-	At	0 15	1001	
	AE	-						We the	1005900	
	AF	-						SCNIE	1/000	
	AG	+					ィレ	HOEN,		
	AH									
	AI	+-								
	AJ AK	+								
	AN			FOR	EIGN PATENT DOCUMENTS	3				
EXAMINER INITIAL		1 -	JMENT	DATE	COUNTRY	C	LASS	SUB- CLASS	TRANSLATION	
		NUM	SER						Yes	
	AL								No.	
				ļ				}	Yes No	
	AM								Yes	
	AN								No	
						ļ			Yes No	
	AO	-						 	Yes	
	AP	i						<u> </u>	No	
	1		OTHER (I	ncluding Autl	nor, Title, Date, Per	tinent Pages,	, etc.)			
	AR	OTHER (Including Author, Title, Date, Pertinent Pages, etc.) Braunwalder, A.F., et al., "Measurement of the Protein Tyrosine Kinase Activity of c-src Using Time-Resolved Fluorometry of Europium Chelates," Anal. Biochem. 238:159-164, Academic Press, Inc. (July 1996)							se Activity . Biochem.	
	AS	2		Buchmann, A., et al., "Progression of Squamous Carcinoma Cells to Spindle Carcinomas of Mouse Skin Is Associated with an Imbalance of H- <i>ras</i> Alleles on Chromosome 7," <i>Cancer Res</i> . 51:4097-4101, American Association for Cancer Research (1991)						
	AT	2	1	Castle, V., et al., "Antisense-mediated Reduction in Thrombospondin Reverses the Malignant Phenotype of a Human Squamous Carcinoma," <i>J. Clin. Invest. 87:</i> 1883- 1888, American Society for Clinical Investigation (1991)						
EXAMINER	L	1				DA	TE CONS	SIDERED		
1										

Page 3 of 19

AUG 0 2 2002

FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO. 0652.1790001/EKS/BEC	APPLICATION NO. 10/086,073
APPLICANTS Beug et al.	
FILING DATE	GROUP

1111	011111101	. 5150	CLOSURE STA		FILING DATE March 1, 2002		GROUP 1642		
	-			U.S.	PATENT DOCUMENTS				
EXAMINER INITIAL		DOCU	JMENT BER	DATE	NAME	CL	ASS	SUB- CLASS	FILING DATE
	AA							1	
	AB				<u> </u>			1	1600,5000 645
	AC							-F/Y	<u> </u>
	AD	↓					at	10 m	685
	AE	 					1,,-	21/62	- 1900 -
	AF	 						1775	180010-
	AG	+-						TOENIE.	
	AH	 					- 7E 1	171,0	-
	AI			 					
	AJ	 		 					
	AK								<u></u>
				FOREIG	GN PATENT DOCUMENTS			1	
EXAMINER INITIAL		DOC!	UMENT BER	DATE	COUNTRY	CL	ASS	SUB- CLASS	TRANSLATION
	AL								Yes No
	AM	1							Yes No
		+							Yes No
	AN	+							Yes No
	AO	+-							Yes No
· ·····	AP			- 31 3	, Title, Date, Pertin	ant Pages	etc)	1	
	AR	<u>3</u>	Caulin, C Cells to	., et al., "C Transforming	Chronic Exposure of Cu Growth Factor-β, Inducand a Spindle Tumoral Association for Cance	iltured Tra ces an Epit Phenotype,	nsforme thelial " <i>Cell</i>	l-Mesenchy <i>Growth D.</i>	mal
	AS	3	Dependent	DeBortoli, M.E., et al., "Amplified Expression of p21 ras Protein in Hormone-Dependent Mammary Carcinomas of Humans and Rodents," <i>Biochem. Biophys. Res.</i> Commun. 127:699-706, Academic Press, Inc. (1985)					
de Brito, P.A , et al., "Carcinosarcoma (Malignant Mixed Müllerian (Mesodern Tumor) of the Female Genital Tract: Immunohistochemical and Ultrastructural Analysis of 28 Cases," Hum. Pathol. 24:132-142, W.B. Saunders Company (1993)							uctural		
EXAMINER		<u>. </u>			<u></u>	DAT	E CONS	IDERED	

EXAMINER

Page 4 of 19 APPLICATION NO. ATTY. DOCKET NO. 0652.1790001/EKS/BEC 10/086,073 FORM PTO-1449 APPLICANTS Beug et al. INFORMATION DISCLOSURE STATEMENT FILING DATE GROUP 1642 March 1, 2002 U.S. PATENT DOCUMENTS EXAMINER FILING DATE CLASS SUB-NAME DOCUMENT DATE INITIAL. CLASS NUMBER AA AB AC AD ΑE AF ΑH ΑI ΑJ ΑK FOREIGN PATENT DOCUMENTS EXAMINER TRANSLATION SUB-COUNTRY CLASS DOCUMENT DATE INITIAL CLASS NUMBER Yes No ALYes ΑM Yes No ΑN Yes No ΑO Yes No ΑP OTHER (Including Author, Title, Date, Pertinent Pages, etc.) Eaton, S., and Simons, K., "Apical, Basal, and Lateral Cues for Epithelial Polarization," Cell 82:5-3, Cell Press (July 1995) AR 4

Transforming Gene of Harvey Murine Sarcoma Virus and of the Cellular ras Gene Family, " J. Virol. 43:294-304, American Society for Microbiology (1982) DATE CONSIDERED EXAMINER

93:2909-2914, National Academy Press (April 1996)

AS

ΑT

4

4

Fakhrai, H., et al., "Eradication of established intracranial rat gliomas by transforming growth factor β antisense gene therapy," Proc. Natl. Acad. Sci. USA

Furth, M.E., et al., "Monoclonal Antibodies to the p21 Products of the

Page 5 of 19



ATTY. DOCKET NO. 0652.1790001/EKS/BEC

APPLICATION NO. 10/086,073

INFORMATION DISCLOSURE STATEMENT

APPLICANTS Beug et al.

					FILING D March 1,			1642		
				Ŭ	.S. PATENT DOC					
EXAMINER INITIAL		DOCU NUME	JMENT BER	DATE	NAME			CLASS	SUB- CLASS	FILING DATE
	AA									
	AB								11/15	100055000
	AC								FIA	
	AD							DK.	V 3	V//
	AE			<u> </u>				\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	196 11	5000
	AF							<u> </u>	T- NIEA	100
	AG					w			CELAL	
	АН							150	<u> </u>	
	ΑI								ļ	
	AJ								ļ	
	AK								<u> </u>	
				FOI	REIGN PATENT D	OCUMENTS		1		
EXAMINER INITIAL		DOC!	UMENT BER	DATE	COUNTRY			CLASS	SUB- CLASS	TRANSLATION
										Yes No
	AL			 				 		Yes
	AM	1								No
	7.11									Yes
	AN							 	 	No
										Yes No
	AO_								-	Yes
	AP								<u> </u>	No
			OTHER (In	cluding Aut	hor, Title, Da	te, Pertiner	nt Pag	es, etc.)		
	AR	<u>5</u>	Guarino, differen (1993)	M., et al. ntiation," <i>H</i>	, "Candinosard Ústopathology	coma of the o 22:493-498,	oesoph Black	nagus with well Scie	rhabdomyo ntific Pul	oblastic olications
	AS	5	Hand, P.H., et al., "Monoclonal antibodies of predefined specificity detect activated ras gene expression in human mammary and colon carcinomas," Proc. Natl. Acad. Sci. USA 81:5227-5231, National Academy Press (1984)							
	AT	Hay, E.D., "An Overview of Epithelio-Mesenchymal Transformation," Acta Anat. 154:8-20, S. Karger Medical and Scientific Publishers (March 1996)							ta Anat.	
EXAMINER								DATE CONS	IDERED	

Page 6 of 19

/	6	1 F		
	AUG	0 2	2002	C78 &
FORM	PTO	7: n F	ARK 19	<i>y</i>

ATTY. DOCKET NO. 0652.1790001/EKS/BEC

APPLICATION NO. 10/086,073

APPLICANTS Beug et al

TNI	CORMATIC	N DISC	CLOSURE ST	ATEMENT	Dodg co di.		т —		······································	
1111	J. 1. 11 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	5150			FILING DATE March 1, 2002 GROUP 1642					
			- 111	U.S.	PATENT DOCUMENTS		1 12			
EXAMINER INITIAL		DOCU	JMENT BER	DATE	NAME		LASS	SUB- CLASS	FILING DATE	
	AA	1,01,11							5 1000:5000 5005	
	AB								EU	
	AC							CEI	- 20	
	AD						BI	 	3000	
	AE							Mr.	3800:5300	
	AF	<u> </u>						37000	R 100	
	AG						- ~	CHOE!		
	AH				<u> </u>			 	 	
	AI	_								
	AJ					-		<u> </u>		
	AK									
· · · · · · · · · · · · · · · · · · ·				FOREI	GN PATENT DOCUMENTS			1		
EXAMINER INITIAL		DOC!	UMENT BER	DATE	COUNTRY	C	LASS	SUB- CLASS	TRANSLATION	
									Yes	
	AL							 	No Yes	
	AM								No	
	AN								Yes No	
									Yes No	
	AO_								Yes	
	AP				<u> </u>				No	
	-		OTHER (In	cluding Author	, Title, Date, Pert	inent Pages,	etc.)			
	AR	<u>6</u>	Heatley, epitheli	M., et al., ' um," J. Clin.	"Vimentin expression Pathol. 46:441-445,	n in benign a BMJ Publish	and mal	ignant bre	east)	
	AS	<u>6</u>	Carcinom	Hoosein, N.M., et al., "Differential Sensitivity of Subclasses of Human Colon Carcinoma Cell Lines to the Growth Inhibitory Effects of Transforming Growth Factor- β 1," Exp. Cell Res. 181:442-453, Academic Press, Inc. (1989)						
	AT	<u>6</u>	Jenkins,	D.C., et al. is," Br. J. Ca.	, "A novel cell-base ncer 68:856-861, Mac	ed assay for cmillan Pres	the ev s, Ltd.	aluation (of anti- <i>ras</i>	
EXAMINER			1			DA	TE CONS	IDERED		
I										

Page 7 of 19



FORM PTC-1449

INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO. APPLICATION NO. 0652.1790001/EKS/BEC 10/086,073 APPLICANTS

Beug et al.

GROUP FILING DATE

					FILING DATE March 1, 20		GROU 1642		· .	
				U	.S. PATENT DOCUME	NTS				
EXAMINER INITIAL		DOC!	UMENT BER	DATE	NAME		CLASS	SUB- CLASS	FILING DATE	
	AA							_	60	
	AB							- <\	164 1600 5800	
	AC							4CV	1	
	AD						1 2		Opport 1	
	AE						`	Mp	72 1890 1500	
	AF							1125	(12 / · · · · · · · · · · · · · · · · · ·	
	AG					44.	 	4FCHON		
	АН	_				· · · · · · · · · · · · · · · · · · ·	<u> </u>	1	-	
	AI			_				_		
	AJ			_						
	AK							<u> </u>		
				FOI	REIGN PATENT DOCUM	MENTS	1	1		
EXAMINER INITIAL			UMENT BER	DATE	CCUNTRY		CLASS	SUB- CLASS	TRANSLATION	
	AL								Ye N	
	AM								Ye. No	
	AN								Yes No	
	AO								Yes No	
	AP								Ye: No	
		-	OTHER (In	cluding Aut	nor, Title, Date,	Pertinent Pa	ges, etc.)			
	AR	7	Kern, F.	.G., et al., ' Semin. Can	"Growth factor recer Biol. 1:317-3:	eceptors and 28, W.B. Saur	the progre	ession of any (1990	breast	
	AS	7	Keski-O	<pre>Feski-Oja, J., et al., "Transforming Growth Factors and Control of Neoplastic Cell Growth," J. Cell. Biochem. 33:95-107, Alan R. Liss, Inc. (1987)</pre>						
	AT	7	61 Gene	Responsive 64:7041-7045	"Promoter Sequen to Transforming G , American Societ	rowth Factor-	·β1 Autoin	duction,"	J. Biol.	
EXAMINER	<u> </u>	1	<u> </u>			- 1000	DATE CON:	SIDERED		



FORM PTO-1449

ATTY. DOCKET NO. 0652.1790001/EKS/BEC_ APPLICATION NO. 10/086,073

APPLICANTS Beug et al.

INFO	RMAT101	N DISC	LOSURE STA	I EMENT	FILING DATE GROUP March 1, 2002 1642					
			1.2	U.S.	PATENT DOCUMENTS					
EXAMINER INITIAL		DOCU NUMB	MENT ER	DATE	NAME	CL.	ASS	SUB- CLASS	FILING DATE	
	AA							-		
	AB								MED	
	AC							BEUL	2 300s	
	AD							0116	72 (1000	
	AE	<u> </u>		···				AO C	= 1800 5000	
	AF							FOH CEN	EH 1600 5000	
	AG							FOLLOW		
	HA	-								
	AI									
	AJ									
	AK							<u></u>		
				FOREIG	N PATENT DOCUMENTS	-		<u> </u>	 	
EXAMINER INITIAL		DOCU	MENT BER	DATE	CCUNTRY	CL	ASS	SUB- CLASS	TRANSLATION	
	AL								Yes No	
	AM								Yes No	
		1							Yes No	
	AN	†	<u> </u>						Yes No	
	AO	 							Yes	
	AP		<u> </u>						No	
	т	. (OTHER (Incl	uding Author,	Title, Date, Pertinent	Pages,	etc.)			
	AR	<u>8</u>	Farnesylt:	., et al., "Se ransferase Inf cement of Scie	elective Inhibition of ranibitor," Science 260:193 ence (1993)	as-Depe: 34-1937	ndent '	Transforma ican Assoc	ation by a riation for	
	AS	<u>8</u>	ras-depend	Kohl, N.E., et al., "Protein farnesyltransferase inhibitors block the growth of ras-dependent tumors in nude mice," <i>Proc. Natl. Acad. Sci. USA 91</i> :9141-9145, National Academy Press (1994)						
	АТ	8	Kohl, N.E., et al., "Inhibition of farnesyltransferase induces regression of mammary and salivary carcinomas in ras transgenic mice," Nat. Med. 1:792-797, Nature Publishing Company (August 1995)						ssion of :792-797,	
EXAMINER	1		•	-		DAT	E CONS	IDERED		

Page 9 of 19

AUG 0 2 2002

FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

	APPLICATION NO. 10/086,073
APPLICANTS Beug et al.	

<u></u>	0	<u></u>	CLUSURE STA		FILING DATE March 1, 2002		GROUP 1642		
				U.S	. PATENT DOCUMENTS				
EXAMINER INITIAL		DOCU NUME	UMENT IBER	DATE	NAME		CLASS	SUB- CLASS	FILING DATE
	AA								<u> </u>
	AB							Ly.	<u> </u>
	AC							L 'K,	1000
	AD						- Pr	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1000
	AE						`	CENTE ONLE	- 1600 c-
	AF							1442 H	*************************************
	AG						٦٢	1400	+
	АН							\times	
	AI							 	
	AJ						 	 	1
	AK			1		1		<u> </u>	
				FOREI	IGN PATENT DOCUMENT:	:s 		Τ	
EXAMINER INITIAL			CUMENT 1BER	DATE	COUNTRY		CLASS	SUB- CLASS	TRANSLATION
	AL	1_							Yes No
	AM								Yes No
	AN								Yes No
	AO		-						Yes No
	AP	+							Yes No
	AF	—	OTED (Inc	_l	r, Title, Date, Per	rtinent Page	etc.)		
	AR	9	LeJeune S	S., et al., "A	Amphiregulin, Epide n Human Primary Bre for Cancer Research	ermal Growth east Cancer,	n Factor I	Receptor, Res.53:3	and Estrogen 597-3602,
	AS	9	Functiona	Lin, H.Y., et al "Expression Cloning of the TGF-β Type II Receptor, a Functional Transmembrane Serine/Threonine Kinase," Cell 68:775-785, Cell Press (1992); erratum, Cell 70:1068, Cell Press (1992)					
	AT	9	Matsui, F Examined Company	. by Immunohist	Lung Carcinoma With tochemistry," Hum.	h Spindle Ce Pathol. 23:	∍ll Compo :1289-129	nents: Si 7, W.B. S	xteen Cases aunders
EXAMINER		1	<u></u>			D	DATE CONS	IDERED	

Page 10 of 19

FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

	APPLICATION NO.
APPLICANTS	
Beug et al.	

FILING DATE GROUP

					FILING DATE March 1, 20		GROU 1642		
				U	.s. patent docume				
EXAMINER INITIAL		DOC NUM	UMENT BER	DATE	NAME		CLASS	SUB CLASS	FILING DATE
	AA								
	AB								WED
	AC							LCK	,,,,
	AD						5	360	2500
	AE							alla	1 2000
	AF								1 E S 1000 5000
	AG							Tech Or	
	AH							VEC.	
	AI								
	AJ								
	AK								
				FOI	REIGN PATENT DOCU	MENTS		1	
EXAMINER INITIAL		DOC NUM	UMENT BER	DATE	COUNTRY		CLASS	SUB- CLASS	TRANSLATION
	AL								Yes No
	AM								Yes No
	AN								Yes No
									Yes No
	AO	 							Yes
	AP				hor, Title, Date,				110
	AR	10	Miettine Epitheli	en, P.J., <i>et</i> al Cells to	al., "TGF-β Indu Mesenchymal Cell , Rockefeller Uni	ced Transdiff s: Involvemen	erentiation	on of Mamm	nary Drs," <i>J. Cell</i>
	AS	10	oligodec mechanis	xvribonucle	, "Sequence-speci otide targeted to in vivo," Proc. mber 1996)	human C-raf	kinase su	pports an	antisense
	AT	10	Murthy, Carcinon	U., et al., na Cell Line	"Expression of Tes," Int. J. Cance	${}^{\circ}$ GF- $lpha/$ EGF and ${}^{\circ}$ 2 r 44:110-115,	TGF-β Fec Alan F.	eptors in Liss, Inc	Human Colon (1989)
EXAMINER		1	1				DATE CON	SIDERED	

Page 11 of 19

FORM PTO-1449

ATTY. DOCKET NO. 0652.1790001/EKS/BEC APPLICATION NO. 10/086,073

APPLICANTS

Beug et al. INFORMATION DISCLOSURE STATEMENT FILING DATE GROUP March 1, 2002 1642 U.S. PATENT DOCUMENTS EXAMINER FILING DATE SUB-CLASS INITIAL DOCUMENT DATE NAME CLASS NUMBER AA AB AC AD ΑE ΑF AG ΑH ΑI АJ ΑK FOREIGN PATENT DOCUMENTS EXAMINER CLASS SUB-TRANSLATION COUNTRY INITIAL DOCUMENT DATE CLASS NUMBER Yes No ALYes No AM Yes No AN Yes No ΑO Yes No OTHER (Including Author, Title, Date, Pertinent Pages, etc.) Nishihara, K., and Tsuneyoshi, M., "Undifferentiated Spindle Cell Carcinoma of AR. the Gallbladder: A Clinicopathologic, Immunohistochemical, and Flow Cytometric 11 Study of 11 Cases, " Hum. Pathol. 24:1298-1305, W.B. Saunders Company (1993) Oft, M., et al., "TGF- β 1 and Ha-Ras collaborate in modulating the phenotypic plasticity and invasiveness of epithelial tumor cells, " Genes Dev. 10:2462-2477, AS 11 Cold Spring Harbor Laboratory Press (October 1996) Parker, T.G., et al., "Peptide Growth Factors Can Provoke 'Fetal' Contractile Protein Gene Expression in Rat Cardiac Myocytes," J. Clin. Invest. 85:507-514, American Society for Clinical Investigation, Inc. (1990) AΤ 11 DATE CONSIDERED EXAMINER

Page 12 of 19

10	PE	
AUG AUG	0 2 2002	
AITHU S	TR: France France	

FOFM PTO-1449

INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO. 0652.1790001/EKS/BEC APPLICATION NO. 10/086,073

APPLICANTS Heug et al.

FILING DATE GROUP March 1, 2002 1642 U.S. PATENT DOCUMENTS EXAMINER FILING DATE INITIAL DOCUMENT DATE NAME CLASS SUB-NUMBER CLASS AA AΒ ACΑD ΑE AF AG AΗ ΑI АJ ΑK FOREIGN PATENT DOCUMENTS EXAMINER TNTTTAL. DOCUMENT DATE COUNTRY CLASS SUB-TRANSLATION NUMBER CLASS Ves ALNo Yes No ΑM Yes No AN Yes AO No Yes ΔP Νo OTHER (Including Author, Title, Date, Pertinent Pages, etc.) Payne, P.A., et al., "An activated c-Ha-ras allele blocks the induction of AR muscle-specific genes whose expression is contingent on mitogen withdrawal," 12 Proc. Natl. Acad. Sci. USA 84:8956-8960, National Academy Press (1987) Quilliam, L.A., et al., "Identification of Residues Critical for Ras(17N) Growth-Inhibitory Phenotype and for Ras Interaction with Guanine Nucleotide Exchange AS 12 Factors, "Mol. Cell. Biol. 14:1113-1121, American Society for Microbiology (1994) Roberts, A.B., and Sporn, M.B., "Mechanistic Interrelationships between Two Superfamilies: The Steroid/Retinoid Receptors and Transforming Growth Factor- β ," ΑТ <u>12</u> Cancer Surv. 14:205-220, Cold Spring Harbor Laboratory Press (1992) EXAMINER DATE CONSIDERED



FORM PTO-1449

ATTY: DOCKET NO: 0552.1790001/EKS/BEC

APPLICATION NO. 10/086,073

APPLICANTS

Beug et al. INFORMATION DISCLOSURE STATEMENT GROUP FILING DATE March 1, 200 1642 PATENT DOCUMENTS U.S. EXAMINER FILING DATE CLASS SUB-DOCUMENT DATE NAME INITIAL CLASS NUMBER AA AΒ AC ΑD ΑE AF AG AΗ ΑI AJ ΑK FOREIGN PATENT DOCUMENTS EXAMINER TRANSLATION CLASS SUB-DOCUMENT DATE COUNTRY INTTIAL CLASS NUMBER Yes No AL Yes No Yes No ΑN Yes No ΑO 7es No AΡ OTHER (Including Author, Title, Date, Pertinent Pages, etc.) Sanford, K.K., et al., Sarzomatous Change and Maintenance of Differentiation in Long-Term Cultures of Mouse Mammary Carcinoma, " J. Natl. Can. Inst. 26:1139-1183, AR 13 U.S. Dept. of Health, Education, and Welfare, Public Health Service, NIH (1961) Sato, Y., et al., "Characterization of the Activation of Latent TGF- β by Cocultures of Endothelial Cells and Pericytes or Smooth Muscle Cells: A Self-AS 13 regulating System," J. Cell Biol. 111:757-763, Rockefeller University Press (1990) Schoenenberger, C.-A., et al., "Integrin expression and localization in normal MDCK cells and transformed MDCK cells lacking apical polarity, " J. Cell Sci. ΑT <u>13</u> 107:527-541, Company of Biologists, Ltd. (1994) DATE CONSIDERED EXAMINER

Page 14 of 19

APPLICATION NO. ATTY. DOCKET NO. 10/086,073 0652.1790001/EKS/BEC FORM PTO-1449 APPLICANTS Beug et al INFORMATION DISCLOSURE STATEMENT FILING DATE GROUP March 1, 2002 1642 U.S. PATENT DOCUMENTS EXAMINER FILING DATE DATE NAME CLASS SUB-DOCUMENT INITIAL CLASS NUMBER AA AΒ AC ΑD ΑE ΑF AG AΗ AΙ ΑJ ΑK FOREIGN PATENT DOCUMENTS EXAMINER SUB-TRANSLATION DATE CCUNTRY CLASS DOCUMENT INTTTAL CLASS NUMBER Yes No ALYes No Yes 110 ΑN Yes No ΑO Yes NO AP OTHER (Including Author, Title, Date, Pertinent Pages, etc.) Schultz-Cherry, S., et al., "Thrombospondin Binds and Activates the Small and Large Forms of Latent Transforming Growth Factor- β in a Chemically Defined AR 14 System," J. Biol. Chem. 269:26775-26782, American Society for Biochemistry and Molecular Biology, Inc. (1994) Slamon, D.J., et al., "Expression of Cellular Oncogenes in Human Malignancies," AS 14 Science 224:256-262, American Association for the Advancement of Science (1984) Sonnenberg, A., et al., "In Vitro Differentiation and Progression of Mouse Mammary Tumor Cells," Cancer Res. 46:5913-5922, American Association for Cancer ΑT 14 Research (1986) DATE CONSIDERED EXAMINER **EXAMINER:** Initial if reference considered, whether or not citation is in conformance with MPEP 609. line through citation if not in conformance and not considered. Include copy of this form with next

communication to Applicant.

Page 15 of 19

FILING DATE

AUG 0 2 2002

DATE

FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

DOCUMENT

AT

EXAMINER

INITIAL

	APPLICATION NO. 10/086,073
APPLICANTS Beug et al.	

CLASS

SUB-

FILING DATE GROUP March 1, 2002 1642
U.S. PATENT DOCUMENTS

INITIAL		NUM	BER	DATE	WANTE		CDADO	CLASS	TIBING DATE
	AA								WIFU
	AB							LCF	1/4/-
	AC							HE.	1, 2000
	AD							200	0000
	AE								FER 1600120
	AF	_						FECH CE	MEB 1600/2900
	AG							1500	
	АН								
	AI								
	AJ								
	AK								
				FOR	REIGN PATENT DOCUME	NTS			
EXAMINER INITIAL		DOC NUM	UMENT BER	DATE	COUNTRY		CLASS	SUB- CLASS	TRANSLATION
	AL								Yes No
	AM								Yes No
	AN								Yes No
	AO								Yes No
	AP								Yes No
			OTHER (In	cluding Auth	nor, Title, Date, P	ertinent Page	es, etc.)		
	AR	<u>15</u>	Activity	of Either (., "Dominant Inhibi Cellular or Oncoger r Microbiology (199	nic Ras," <i>Mol</i>			
	AS	<u>15</u>	Spindle	Cell Carcino	., "The Conversion omas Is a Recessive ity Press (1993)				
		1	1						

NAME

EXAMINER DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

Thompson, A.M., et al., "Transforming growth factor $\beta 1$ is implicated in the failure of tamoxifen therapy in human breast cancer," Br. J. Cancer 63:609-614, Macmillan Press, Ltd. (1991)



FORM PTO-1449

ATTY. DOCKET NO. 0652.1790001/EKS/BEC APPLICATION NO. 10/086,073

APPLICANTS Beug et al.

NUMBER AA AB AC AD AE AF AG AH AH AI AI AJ AK FOREIGN PATENT DOCUMENTS	FILING DATE
EXAMINER INITIAL DOCUMENT NUMBER DATE NAME CLASS SUB-CLASS FOR THITIAL DOCUMENT NUMBER DATE NAME CLASS SUB-CLASS FOR THITIAL DATE CLASS SUB-CLASS FOR THITIAL DOCUMENT DATE COUNTRY CLASS SUB-CLASS FOR THITIAL DOCUMENT DATE COUNTRY CLASS SUB-CLASS TAME AAA AAA AAA AAA AAA AAA AAA AAA AAA	
INITIAL DOCUMENT NUMBER DATE NAME CLASS SUB-CLASS FARMINER INITIAL DOCUMENT DATE COUNTRY CLASS SUB-CLASS TAME AAA CLASS FACE CLASS	
AA AB AB AC AC AC AD AC AC AD AC	1ED
AH AI AI AJ AJ AK	+ + 900 5 5 3 0 0
AH AI AI AJ AJ AK	} 1,600. 5900
AH AI AI AJ AJ AK	1 1600 5 300
AH AI AI AJ AJ AK	+ 1000.5200
AH AI AI AJ AJ AK	7.00
AH AI AI AJ AK FOREIGN PATENT DOCUMENTS EXAMINER ENITIAL AL AM AN AN AN AN AP AP	
AH AI AI AJ AX AK	
AJ AK COUNTRY CLASS SUB-CLASS TAN AN AO AP	
AK DOCUMENT DOCUMENT NUMBER DATE COUNTRY CLASS SUB-CLASS TAMINER AN AN AN AN AP AP	
EXAMINER INITIAL DOCUMENT NUMBER DATE COUNTRY CLASS SUB-CLASS TABLE AN AO AP AP	
EXAMINER INITIAL DOCUMENT NUMBER DATE COUNTRY CLASS SUB-CLASS TABLE OF THE CLASS SUB-CLASS SUB-CLASS TABLE OF THE CLASS SUB-CLASS SUB-CLASS TABLE OF THE CLASS SUB-CLASS SUB-CLASS TABLE OF THE CLASS SUB-CLASS SU	
INITIAL DOCUMENT NUMBER DATE COUNTRY CLASS SUBCLASS AL AM AN AO AP	
AN AO AP	TRANSLATION
AN AO AP	Yes No
AO AP	Yes No
AO AP	Yes No
AP	Yes
	Yes
	
AR 16 Thompson, T.C., et al., "Transforming Growth Factor βl as a Biomarker f Prostate Cancer," J. Cell. Biochem. 16H (Suppl.):54-61, Wiley-Liss, Inc.	for nc. (1992)
AS Lippincott Company (1993) Thompson, T.C., et al., "Transgenic Models for the Study of Prostate Cancer 71 (Suppl.):1165-1171, J.B. Lippincott Company (1993)	Cancer,"
Thorburn, A., et al., "HRas-dependent Pathways Can Activate Morphologic Genetic Markers of Cardiac Muscle Cell Hypertrophy," J. Biol. Chem. 268 2249, American Society for Biochemistry and Molecular Biology, Inc. (19	68:2244-
EXAMINER DATE CONSIDERED	

Page 17 of 19

AUG 0 2 2002

FORM PTO-1449

ATTY. DOCKET NO. 0652.1790001/EKS/BEC APPLICATION NO. 10/086,073

APPLICANTS

	ODMANTA	N DIC	or compr. a	m a millianda	APPLICANTS Beug et al.				
INF	ORMATIC	N DIS	SCLOSURE S	TATEMENT	FILING DATE GROUP				
	 			υ.	March 1. 200 S. PATENT DOCUMEN		1642		
EXAMINER INITIAL			UMENT BER	DATE	NAME		CLASS	SUB- CLASS	FILING DATE
	AA								
	AB								WED
	AC						1	REUE	1100
	AD							* ** NE (5 200%
	AE				- in			, פטע	ER 1600/2900
	AF						ļ	JOY CENT	EH 1000,500
	AG						\	1401105	
	AH								ļ
	AI						ļ	.	
	AJ								
	AK			_				<u> </u>	
				FOR	EIGN PATENT DOCUM	ENTS		·· •	
EXAMINER INITIAL			UMENT BER	DATE	COUNTRY		CLASS	SUB- CLASS	TRANSLATION
									Ye
	AL						+		N ₁
	AM								Ye N
		1							Ye
	AN								N
	7.0								Ye N
	AO		···						Ye
	AP								No.
			OTHER (In	cluding Auth	or, Title, Date,	Pertinent Pag	es, etc.)		
	AR	<u>17</u>	Vogelste Genet. 9	in, B., and 1:138-141, El	Kinzler, K.W., "T sevier Science Pu	he multistep blishers, Ltd	nature of 1. (1993)	cancer,"	Trends
	AS	<u>17</u>	Wargotz, Carcinos	E.S., and N arcoma," <i>Can</i>	Jorris, H.J., "Met acer 64:1490-1499,	aplastic Carc	cinomas of cott Compa	the Breasiny (1989)	st. III.
	AT	<u>17</u>	adenocar	cinoma cell	"Transforming gr invasion and meta tional Academy Pr	static potent	S stimulat	es mammary	Y Acad. Sci.
EXAMINER		L					DATE CONS	IDERED	

Page 18 of 19



FORM PTO-1449

APPLICATION NO. ATTY. DOCKET NO. 0652.1790001/EKS/BEC 10/086,073

APPLICANTS

****		N DIG	ar caupp am	P. (T.) 1. N. 4. 1. 3. 1 (T.)	APPLICANTS Beug et al.				
INF	ORMATIC	N DIS	CLOSURE ST	ATEMENT	FILING DATE March 1, 2002	GROUP 1642			
		 .		บ. ร	. PATENT DOCUMENTS		11047		
EXAMINER INITIAL		DOC NUM	UMENT BER	DATE	NAME		CLASS	SUB CLASS	FILING DATE
	AA								
_	AB								EV
	AC							130	
	AD								1011
	AE		-				<u> </u>	<u> </u>	300,7
<u> </u>	AF'							VOC	12 1000
	AG		76-31-18-					27 (5,4)	
	АН						•	1 Cur	# 1020 5003
	AI							<u> </u>	
	ΑJ								
	AK.								
				FOREI	GN PATENT DOCUMENTS			1	
EXAMINER INITIAL		DOC NUM	UMENT BER	DATE	COUNTRY		CLASS	SUB- CLASS	TRANSLATION
	AL								Yes No
	AM		·						Yes No
	AN								Yes No
	A O								Yes No
	AP								Yes No
			OTHER (Inc	luding Author	, Title, Date, Pertine	nt Page:	s, etc.)		
	AF:	<u>18</u>	Whitman M induction	., and Meltor ," <i>N</i> ature 357	n, D.A., "Involvement o 7:252-254, Macmillan Pu	of p21 ^{ris} ablisher	in <i>Xeno</i> s, Ltd.	<i>pus</i> mesode (1992)	rm
	AS	<u>18</u>	Malignant	and Benign E	Thrombospondin and Othe Breast Disease. An Immu American Association	unohisto	chemical	Study," A	
	AT	<u>18</u>			'TGF; Signals through a 3-1014, Cell Press (199		meric Pr	otein Kina	se Receptor
EXAMINER	L	1	1		7-9	D.	ATE CONS	IDERED	

		\3	· <u>.</u>	٠,٣					P	age 19 of 19			
	TRANSPORT						ATTY. DOCKET NO. APFLICATION NO. 10/086,073						
•		FORM 1	PTO-1449			APPLICANTS	· · · · · · · ·	1 /					
INF	ORMATIO	ON DIS	CLOSURE S	TATEMENT		Beug et al. FILING DATE		GROU	p				
						March 1, 2002		1642					
	<u> </u>	I		<u></u>	J.S. P	ATENT DOCUMENTS	S	1	· T	1			
EXAMINER INITIAL		DOC NUM	UMENT BER	DATE		NAME		CLASS	SUB- CLASS	FILING DATE			
	AA									(C)			
	AB								ECE	150			
	AC	_						1 p	FULL	EK 1600/5800			
	AD							\ \ \	3116	- Spans			
Addr.	AE								140.	ER 1600/200			
- 1 to 1 and	AF			-	-+				- HUEM				
	AG AH	+						1 7	1401,				
	AI							<u> </u>					
	AJ	-				·							
	AK				İ								
		•		FO	REIGN	PATENT DOCUMEN	TS			-			
EXAMINER INITIAL		DOC NUM	UMENT BER	DATE		COUNTRY		CLASS	SUB- CLASS	TRANSLATION			
	AL									Yes No			
	AM									Yes No			
	AN									Yes No			
	AO									Yes No			
	AP									Yes No			
			OTHER (In	cluding Aut	hor, :	Title, Date, Pe	rtinent Pa	ges, etc.)					
	AR	<u>19</u>	Wrana, J 370:341-	.L., et al. 347, Macmil	, "Me lan P	chanism of acti ublishers, Ltd.	vation of (1994)	the TGF-3	receptor,	" Nature			
	AS	19	Receptor Human Ke	s and Induc ratinocytes	es the	ransforming Groe e de novo Expre lications for W ress (May 1995)	ession of t Nound Heali	he ανβ6 He	eterodimer	in Normal			
	AT	<u>19</u>		ional Searc uly 18, 199		ort for Interna	ational App	lication 1	No. PCT/EP	97/01699,			
EXAMINER		<u> </u>	<u> </u>				<u></u>	DATE CONS	SIDERED				

Sterne Kessler Goldstein Fox



and the state of the state of the state of	
pitAanti kenilen	
tripe A in 155 ent	
Tay 1 K I HAR	
Autort & Exmand	
Trail General Comm	
the seek a leading	
Militae B. Ray	
A representation of the	
1 2ette	
ممد ي شوط اوا	
Stephen Book dwill	
معميرة فيعادون	
Land Alleger	
المرافية العبيرة يرا	
The state of the s	
Lisabet ett tillt i Lisati Skatta fis	

10 mg - 12 mg - 1
Egro & F. Green
الجراعي والأكثر التكالم
med. Ma.
Settle 18 mm
Edward Allen
All port of port of
Consideration
eeter Alija kirjar
보다 가장 보다 됩니다.
en die Mede
المرجاجي كالمنافق
Tenton to Pater
and the section of th
51.00
and the second second
A 50 8 A15

erar Televis
ing the Bells on the
Regradicula
x mper y N. Reddini
Thurst Hald Assess
Fladett Hadin
er viele il fraiker
e; • • • • • • •
Frank A. Hinghan
nak yorangamar
Act of the photo see
awser e arrist
e spot Baldteroo
- 1 mg - 15 gr

i 🌽 i k 2 d - Yi k 1 - 💋 k
Fred B. Makha 2
Anthes, Kanage
Name of the Property
Arr E. Summerfally
merica, mari
ativ TripA "
Matmew Drwd
Harini, Nifikamo
At gerigue comis
Birlio A. Matuera
Marketina
ngtong ki Pe
Angelon Berlin
and the second of the second of

a A Curren

Admired in Confidence

* Admired in Confidence

* Confiden

August 2, 2002

WRITER'S DIRECT NUMBER: (202) 371-2630 INTERNET ADDRESS: behalker a skgf.com

Commissioner for Patents Washington, D.C. 20231



Art Unit 1642

Re: U.S. Utility Patent Application

Appl. No. 10/086,073; filed March 1, 2002

For: Pharmaceutical Compositions for Treating Tumour Diseases

Inventors: Beug et al.

Our Ref: 0652.1790001/EKS/BEC

Sir:

Transmitted herewith for appropriate action are the following documents:

- 1. Information Disclosure Statement:
- 2. Form PTO-1449 (19 sheets) and accompanying (62) references; and
- 3. Return postcard.

It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier. In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

Commissioner for Patents August 2, 2002 Page 2

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

B-E. Clubber

Bruce E. Chalker Attorney for Applicants Registration No. 47,480

BEC/dab BODMA MHODMA SKGF DC4,41251.1 Enclosures